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Systemic Lupus Erythematosis and Adverse Pregnancy out Come - A Prospective Study

Authors
C. Jayakumari[1], Nirmala.C[2], Shahida J[3], Sujatha Y[4]
[1]Associate Professor of Medicine, Dept. Of Endocrinology, Govt.Medical College, Trivandrum
[2]Professor,Dept of Obstetrics and Gynaecology, Govt.Medical College, Trivandrum.
[3]Associate Professor, Dept of Obstetrics and Gynaecology, Govt.Medical College, Trivandrum.
[4]Professor, Dept of Obstetrics and Gynaecology, Govt.Medical College, Trivandrum.
Corresponding Author
Nirmala.C
Email: *drnirmalatvm@gmail.com*

Abstract
Background: *Systemic lupus erythematosus (SLE) is one of the most common autoimmune disorders that affect women during their childbearing years. It is an idiopathic chronic inflammatory disease that affects skin, joints, kidneys, lungs, serous membrane, nervous system, liver and other organs of the body. SLE increases the risk of spontaneous abortion, intrauterine fetal death, preeclampsia, intrauterine growth retardation, and preterm birth*
Objective: *The Primary objective of the study was to find out the maternal and fetal outcome of SLE complicating pregnancy and diagnosed prior to pregnancy.*
Methodology: *This study was conducted in the Department of Obstetrics and Gynecology in, S.A.T hospital in Govt. Medical College Trivandrum, Kerala in collaboration with the Department of Medicine. This was a prospective follow up study. 36 pregnant women were recruited based on diagnosis of SLE prior to pregnancy.*
Results: *SLE is associated with high proportion of maternal and fetal morbidity and mortality.. 27.8% of cases had preterm labour. There was one case of maternal mortality due to intra cerebral thrombosis. Rate of caesarean section is 56.7%, which is significantly higher than average. IUGR, Intra uterine death and low birth weight were also significantly higher.*
Conclusion: *We conclude that mother with SLE has a significantly higher risk of obstetric and fetal complication including mortality, in spite of the fact that they were on treatment prior to getting pregnant. Multidisciplinary, tertiary care centres equipped with Obstetric critical care unit is essential to improve outcomes.*
Keywords: *SLE, Pregnancy outcome, IUGR, Pre eclampsia, fetal outcomes.*

Introduction

Systemic lupus erythematosus (SLE) is one of the most common autoimmune disorders that affect women during their childbearing years. It is an idiopathic chronic inflammatory disease that affects skin, joints, kidneys, lungs, serous membrane, nervous system, liver and other organs of the body. SLE increases the risk of spontaneous abortion, intrauterine fetal death, preeclampsia, intrauterine growth retardation, and preterm birth.[1,2,3,4]

Autoimmune disorders (AID) in general are 6 to 10 times more common among women than men,. More than 70% of patients with Auto immune disease are women of reproductive age, Studies in both animal models and human support the role of sex hormones play in the development of auto immunity, oestrogen accelerates the disease and androgen are protective. Most AIDs occur frequently in women and should they appear at childbearing age, they pose a potential risk for almost all aspects of reproduction, from fertility to pregnancy itself [4–8]. In the past, it was suggested that women with certain AIDs [particularly systemic lupus erythematosus (SLE) should avoid pregnancy. Currently, due to available treatments and specialized care for pregnant women with SLE, the prognosis for both mother and child has improved significantly [4, 7, 9].

With advances in the medical care of women with auto immune diseases like SLE, many are becoming pregnant. Thus auto immune diseases pose a great threat to the health and well being of pregnant women and their unborn and new born babies. Pregnancy associated fluctuations in sex hormones may influence disease severity. The effect of pregnancy depends on whether auto immune diseases innate (cellular) or adaptive (humoral) in nature. Diseases with strong cellular pathophysiology such as rheumatoid arthritis (RA) and multiple sclerosis are associated with remission during pregnancy and diseases characterized by auto antibody production such as systemic lupus erythematosis (SLE) shows increased severity.

Hence it is important for the obstetrician to be familiar with the common auto immune diseases during pregnancy, how they influence and are influenced by pregnancy and the risks to the mother and foetus due to auto immune diseases. The auto immune diseases commonly seen are systemic lupus erythematosis, immune thrombocytopenic purpura, Type I Diabetes mellitus, myasthenia gravis, etc. It is also seen that adverse pregnancy out comes like abortions spontaneous intra uterine deaths, abruption, preterm labour, IUGR, gestational hypertension etc are more common in these group of patients. The magnitude of the problem largely is unknown in developing countries. Appropriative treatment and early identification of complications can reduce mortality and morbidity to a great extent.

Rationale of the Study

Systemic lupus erythematosus (SLE) is one of the most common autoimmune disorders that affect women during their childbearing years. SLE increases the risk of spontaneous abortion, intrauterine fetal death, preeclampsia, intrauterine growth retardation, and preterm birth. This is very well recognized now that a myriad of clinical manifestations can occur in SLE. Obstetric manifestations including recurrent miss carriages, early onset of preeclampsia, intra uterine growth restriction, abruption in these diseases. These patients are at increased risk of recurrence of complications in subsequent pregnancies. The risk of subsequent pregnancies looses and thrombotic complications are very high in SLE.

Complications like congenital anomalies, miscarriages, intra uterine deaths etc are very commonly associated .Many of these cases can result in good obstetric outcomes in presence of multi disciplinary approach and good ante natal care. There are only very few studies conducted on these diseases., Sree Avittom Thirunnal Hospital (SATH) being a referral centre, all cases of SLE will be referred. This, being a descriptive study a complete understanding of the disease process may not be obtained.

The state of Kerala, the southernmost state of India could achieve health in the indices in par with developed countries. Over the past several years, Kerala is undergoing health transition with emerging of new diseases particularly auto immune diseases. Though the Kerala's maternal mortality is lowest in India and death due to haemorrhage is lowest in the State, emerging newer diseases contributing to maternal mortality is a major challenge to the treating physicians. Hence it is important to study the pregnancy

characteristics and outcome of SLE in pregnancy so that proper intervention can be planned. This study is first of its kind in this tertiary care centre. Hence this study is done with the objectives to study the maternal and fetal outcomes of SLE in pregnancy

Methodology

This study was conducted in the Department of Obstetrics and Gynaecology in the Govt. Medical College Trivandrum, Kerala in collaboration with the Department of Medicine. This was a prospective follow up study. All consecutive cases of pregnant women with SLE were included in the study. Cases were identified from the medical records in the department of Medicine. Those pregnant women with systemic Lupus erythamatosus – who were diagnosed prior to pregnancy and were on treatment, were included in the study. Their pregnancy was registered in the antenatal clinic of the department of Obstetrics and Gynaecology. They were followed up with routine antenatal care and in consultation with the physician in the department of Medicine. All were followed up till delivery. Ethical clearance was obtained from Institutional Ethical committee.

A total of 36 cases of SLE diagnosed prior to pregnancy and were on treatment and registered in the antenatal OP during the study period of one year. After getting informed consent, a detailed history regarding age, socioeconomic status, menstrual and obstetric history were obtained using a structured questionnaire. Details related to duration of disease, hospitalization, complications and treatment were also collected. The data related to disease was also collected from the medical records in the department of medicine. A through general physical examination was carried out during each visit. Ultra sound examination was done between 11-14 weeks for accurate dating and to rule out anomalies. Scans were repeated at 18-20 weeks to rule out other structural anomalies. Biophysical profile for foetal well being was done from 26th week of gestation. Uterine artery Doppler to predict early onset preeclampsia was also done.

Maternal outcome studied were early pregnancy loss, pre-eclampsia, gestational hypertension, gestational diabetes, thrombosis , flare up of SLE, abruption Placenta, pre-term labor, mode of delivery, postpartum hemorrhage, puerperal trom-bosis, puerperal fever. Foetal outcome studied were early pregnancy loss, foetal abnormalities, foetal growth restriction, intra uterine death, gestational age in birth, birth weight, still birth, Meconium aspiration, admission to nursery.

The data was entered cleared and analyzed using SPSS .version 16. We calculated the the mean and standard deviation for continuous variables and proportion for other parameters.

Results

The Socio demographic characteristics and clinical characteristics are shown in table1. Out of 36 cases studied, mean age was 26.3 years, and majority belonged to low Socio economic status. Majority (69.4%) were from rural areas

Table 1- Socio demographic characteristics

Study variable		Frequency	Percentage
Age	<30 yrs	24	66.6
	>30 yrs	12	33.4
Religion	Hindu	24	66.7%
	Muslim	7	19.5%
	Christian	5	13.6%
Parity	Primi	8	22.2%
	G2	12	33.3%
	>G3	16	44.5%
Socio economic status	High	8	22.3%
	Miiddle	8	22.3%
	Low	20	54.4%
Educational Status	High school	30	85.1%
	College	6	13.9%
Place of Residence	Rural	25	69.4%
	Urban	11	30.6%

Majority belonged to Hindu Religion (66.7%) which co relates with the normal distribution of religion in Kerala. 22% of cases were primi gravid and rest was multigravidas with one or more previous pregnancy losses.

Distribution based on duration of disease and treatment shown in table 2.

Table 2 Distribution based on Duration of disease

Duration of disease	N	%
< 6 months	6	16.7
6 months to 1 year	13	36.1
- 2 year	8	22.2
2 year	9	25
Onsteroid Therapy	24	66.6
On Steroids and Heparin	12	33.4

All cases were diagnosed prior to pregnancy and were on treatment. Out of 36 cases of SLE 24 cases were on steroid therapy and 12 were on steroid and heparin Therapy. Majority of cases had disease duration more than one year.

Maternal outcomes are shown in table 3

Table. 3 Distribution of Maternal outcomes

	Variables	No:	%
1.	Gestational Hypertension	10	(27.2)
2.	Pre eclampsia	6	(16.6)
3.	GDM	4	(11.1)
4.	Preterm Labour	16	(44.4)
5.	GDM+ Hypertension	5	(13.8)
6.	Thrombosis	4	(11)
7.	PPH	2	(5.6)
8.	Maternal death	1	(2.8)

27.8% cases developed gestational hypertension and early onset of preclampsia. 13.9% developed gestational hypertension and gestational diabetes. One case of SLE had flareup and died due to intra cerebral thrombosis.11.1 % cases developed thrombosis. Preterm labor was seen in 27.8 % of cases. Post partum haemorrhage was seen in 2 cases .. Cesarean section rate was 56.7 % is significantly higher than average.

Table- 4. Fetal outcomes

	Variables	N	%
1	Spontaneous abortion	6	(16.7)
2	Intrauterine growth restriction	18	50
3	Intra uterine death	2	(6.2)
4	Preterm	10	(27.8)
5	Low birth weight	16	(44. 4)

Table 4 shows the distribution of fetal outcomes 16.7% of cases had spontaneous abortion. There were 2(6.2%) intra uterine fetal death 50% developed IUGR, pre valence of low birth weight was 44.4%

Discussion

Studies related to outcomes pregnancy in those cases of SLE diagnosed prior to pregnancy and on treatment is few in our state and hence this study provided an unique opportunity to find out fetal and maternal outcomes of SLE in pregnancy. Due to the technological developments many women with diagnosed auto immune diseases are conceiving. Finding of the present study is that 77.8% were multi gravidas .Among these multi gravidas, 71.4% had previous history of abortion and 42.8% had previous history of two or more abortions. It was seen that 50% of these patients had disease duration of two or more than two years. Out of SLE patients 25% had flare and 6(16.7%)of them ended up in miscarriages, In a study by Chen et al, it was seen that foetal prognosis depends mostly on disease activity , with foetal loss ranging from 25% to 52% in patients with active SLE when compared to 8 to 12 % in patients with inactive SLE at the onset of pregnancy. The later is comparable to observant-ions in healthy women. out of 36 cases only 5 cases,(17.8%) had a previous successful birth outcome.24 cases (66.6%) were on steroid therapy rest were on steroids and heparin.

Hypertensive disorders were the commonest morbidity. Most commonly reported complication was gestational hypertension (27.7%). The median rate of gestational hypertension /preeclampsia in pregnancy is complicated by SLE is 32%, with range up to 50%[15,16.] It appears that between 20% and 30% of women with SLE develop either gestational hypertension or preeclampsia (gestational hyper tension with proteinuria)[8,9] .Out of the patients with both GDM and GHTN 405 were SLE patients. During pregnancy, chronic glucocorticoid therapy has also been associated with an increased risk of glucose intolerance. [13-16]

Mok et al studied 91 pregnancies ,reporting that anti phospholipids antibodies were more prevalent in patients with recurrent miscarriages and the strongest predictive factor was the presence of lupus anti coagulants.[4] One third of the patients have APS secondary to systematic lupus erythematosis.

Pre term deliveries are found in 27.4% cases which is high compared to normal pregnancy. Among them 80% were above 34 weeks of gestation. Dhar et al reviewed 16 studies on pregnancy out comes before and after the diagnosis of SLE and found that in spite of some limitations in study design and statistical analysis and variations in technology uses, most studies concluded that pregnancy loss, pre term birth and IUGR were more common after than before the diagnose of SLE and compared to control population. The reported incidence of varies. Preterm birth had been reported in as few as 3% and as many as 73% of pregnancies complicated by SLE.

Another significant fetal outcome is the high rate of low birth weight. Among the patients 53.3% of the babies had birth weight less than 2.5 Kg. out of them 50% had SLE. 37.5% of them were preterm babies. Uteroplacental insufficiently resulting in IUGR or small-for-gestational-age neonates occurs in between 12% and 40% of pregnancies with SLE. In the study it was observed that the duration of the disease increased, the associated with adverse outcome increased. There is general agreement that in SLE pregnancy outcomes are more likely to be complicated. The major limitation of the study is that it is a descriptive study and there is comparison group.

Conclusion

Based on our study we conclude that SLE pose great threat to life and well being of pregnant women. They also contribute to significant perinatal mortality & morbidity. Hence a critical care Obstetric unit where a multi disciplinary team care involving Obstetrician, Physician, Obstetric critical care specialist, Hematologist etc are with facilities for high dependency care is essential, to improve outcomes and optimize their obstetric future.

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